SULFATE WHICH CAN BE DERIVED FROM SULFATED ESTROGENS ENHANCES THE 2,3-DIPHOSPHOGLYCERATE CONTENT OF PLACENTA EXPOSED RED BLOOD CELLS. GW Moll,Jr., G Chien Liu* & G Liu Lin*, Department of Pediatrics, University of Mississippi Medical Center, Jackson, Mississippi.

Fetal growth parameters are highly correlated with maternal red blood cell (RBC) 2,3-diphosphoglycerate (DPG) content. We have demonstrated the ability of estrone sulfate (ES) to enhance the DPG content of the placenta exposed RBC. Since the fetal adrenal is a major secretor of sulfated steroids with the placenta capable of releasing their sulfate (SO_4) moiety, we tested the hypothesis that SO_4 can enhance the DPG content of the placenta exposed RBC.

Human full term placenta explant cultures (0.4-0.5g/plate) were rapidly established following delivery and exposed to media(RPMI1640) ± 12ng/ml ES, 1mM SO_4 or 5mM SO_4 for 18h prior to replacement of the incubation media with 2ml washed nonpregnant adult human blood to continue incubation for 4h ± placenta explants (PE) prior to analysis of DPG content by standard 340nm UV spectrophotometric assay (Sigma).

DPG Content (umol/ml±SEM,n=3-6,*p<.01 vs +PE,**p<.01 vs -PE)

Incubation	+PE	-PE
Media alone	1.20 ± 0.03	1.40 ± 0.01 *
18h/4h 5mM SO_4	1.39 ± 0.04 *	1.65 ± 0.01 *, **
Media/4h 1mM SO_4	1.31 ± 0.04 *	1.50 ± 0.02 *
Media/4h 5mM SO_4	1.51 ± 0.01 *	1.80 ± 0.03 *, **

SO_4 significantly enhanced the DPG content of the RBC ± PE.

We conclude that SO_4 can enhance the DPG content of the placenta exposed RBC. The results of this study suggest an important role for interaction of fetal adrenal sulfated steroids with the placenta to support adequate oxygen transfer from the maternal circulation to the Fetal-Placenta unit to permit normal fetal growth and development.

HEALTH CARE

Subspecialty Session

Thursday, January 31, 1991
2:00 PM

O'Hare Room

DEHYDROEPIANDROSTERONE: AN ANTIGLUCOCORTICOID IN YOUNG OBESE ZUCKER RATS. Bruce E. Wright, Johnny R. Porter** and Frank Svec**, Depts. of Physiology and Medicine, LSU Medical Center, New Orleans, LA.

The Zucker rat is an animal model of genetic obesity characterized by hyperphagia, hyperinsulinemia and hyperglycemia (especially in older animals). A variety of evidence implicates the adrenal gland in the genesis and maintenance of the obesity. For example, we have confirmed hypercorticosteronemia in this animal. Likewise, adrenalectomy reverses the above findings. Others have shown that dehydroepiandrosterone (DHEA) given orally corrects these conditions. The mechanism of action of DHEA is unknown. We propose that DHEA acts as an antiglucocorticoid in the Zucker fatty rat. To test this hypothesis we examined the induction by dexamethasone (i.p. 5 ug/100gm body weight) of tyrosine aminotransferase (TAT) in hepatic tissue. Obese male and female rats aged 6-10 weeks were used in all experiments. Following dexamethasone injection, TAT levels were elevated from 1-5 hrs. In a separate study we noted that exogenous DHEA-S given i.p. reached peak values 20 minutes after injection and were still elevated at 80 minutes. When dexamethasone was injected with or without DHEA (500 ug/100 g body weight) we found that dexamethasone induced TAT 5 hrs later and DHEA inhibited this induction (range 50-75%). DMSO, the vehicle, served as a control. DHEA alone did not induce TAT. This assay was done on both kidney and liver homogenates. We observed similar results using ornithine decarboxylase (ODC) as a marker of dexamethasone induction. We conclude that DHEA is an antiglucocorticoid in the young obese Zucker rat and that its chronic antiobesity effect may reflect a chronic antiglucocorticoid activity.

PREDICTORS OF FAILURE TO THRIVE IN LOW BIRTH WEIGHT AND PRETERM INFANTS Kelleher K, Casey P, Bradley R*, Swanson M, Whiteside L*, Whitmarsh K*. Infant Health and Development Program, Department of Pediatrics, University of Arkansas Medical Sciences, Little Rock, AR

This study examined prospectively collected perinatal demographic, maternal and child characteristics to identify risk factors for the development of failure to thrive (FTT) among 985 low birth weight (LBW) and preterm (PT) infants recruited from nurseries in an 8 site collaborative research program.

Using a conservative definition, 121 children met the criteria for FTT, making prevalence of FTT in these LBW children 12.3% with peak prevalence at 12 months. 143 additional children met only 1 criteria and were eliminated from analyses. Incidence rates peaked at 8 months with an overall incidence rate of 13.1%. 78 cases of FTT were diagnosed before 12 months (early onset) while 43 cases were diagnosed between 12 and 24 months. Early onset cases were more likely to be organic in nature (33%) than late onset cases (20%).

Children who developed FTT were 2.4 times more likely to have been SGA than children without FTT (95%CI=1.75,3.40), 1.6 times more likely to have been considered abnormal on neurological examination at 40 wks (1.21,2.21), 1.77 times more likely to have birth weight less than 2000g (1.20,2.59) 1.54 times more likely to have head circumference/BMI ratio greater than normal (1.07,2.20) and 1.64 times more likely to have a mother under 21 (1.17,2.29). A logistic regression model was estimated. After controlling for other predictors, infants were more likely to develop FTT if they were SGA, had an abnormal neurological exam at 40 wks, had a teenage mother or had a mother with post graduate education. Birth weight approached but did not achieve significance in our regression model after controlling for other factors.

The high prevalence and incidence of FTT in LBW infants generated with this conservative definition for FTT supports previous anecdotal reports of greater risk of FTT in LBW & PT infants. Implications for prevention and intervention strategies in LBW & PT infant cohorts will be discussed.

CONTROL OF CUSHING'S SYNDROME SECONDARY TO ECTOPIC ACTH WITH OCTREOTIDE. RV Clark**, RM York*, RM Lauer*, NS Melch, Jr*, Departments of Medicine, Emory University and Piedmont Hospital, Atlanta, GA.

We report 2 patients with hypercortisolism secondary to ectopic ACTH who responded to treatment with somatostatin analog, octreotide. Both patients presented with Cushingnoid habitus, marked weakness, weight loss, hypertension, hypokalemia, and hyperglycemia. The first was a 40 y/o F, urinary free cortisols (UFC) were 6,000-13,000 mcg/24h and ACTH 280-350 pg/ml. Abdominal CT showed extensive liver masses with normal pancreas. The second was a 60 y/o F, UFC were 5,000-7,000 mcg/24h and ACTH 140-200 pg/ml. CT of abdomen showed mass in head of pancreas, and 3 liver metastases. Liver biopsy in the first showed a neuroendocrine type carcinoma possibly islet cell: the second was similar but more acinar like. Chemotherapy for the first with 5FU and streptozotocin was ineffective. Octreotide, 100-250 mcg tid, reduced UFC to 600-800 mcg/d. Addition of ketoconazole, 800-1200 mg/d normalized UFC and resolved all signs and symptoms. Chemotherapy for second with 5FU, adriamycin, and mitomycin induced tumor shrinkage and reduced UFC to 200-300 mcg/d. Octreotide, 100 mcg tid, normalized UFC to 30-70 mcg/d and resolved all symptoms. In both cases, reduction of dose amount or frequency of octreotide resulted in elevated UFC and hyperglycemia. We conclude that octreotide can be effective in controlling ectopic ACTH production and hypercortisolism from neuroendocrine carcinomas.

UNDERSTANDING THE DEVELOPMENT OF FAILURE TO THRIVE IN A LOW BIRTH WEIGHT, PRETERM COHORT: A PROSPECTIVE CONTROLLED STUDY. Patrick Casey, Kelley Kelleher, Robert Bradley, Mark Swanson, Leanne Whiteside, Kathleen Whitmarsh. Department of Pediatrics, University of Arkansas for Medical Sciences.

The development of failure to thrive (FTT) was assessed in a prospective study of low birthweight (LBW) preterm (PT) infants to avoid methodologic problems of previous retrospective research. 985 infants (birth weight ≤ 2500 g, gestation age ≤ 37 weeks) were recruited in the nursery in an 8 site collaborative program. All infants received routine follow-up care at standard intervals, and a broad range of infant, parent, and environmental data were collected in the nursery and at 40 weeks, 4, 8, 12, 18, and 24 months gestation corrected age. 121 infants were clinically diagnosed as FTT by standard definition, and secondarily confirmed by computer mathematical model in the first 24 months of life. 143 infants were considered false positives as they met only 1 criteria. T test analyses compared all independent variables between 121 FTT and 721 non-FTT infants. Of all the maternal and environmental variables, only the total HOME Inventory and its Responsivity and Play Materials subscales differentiated the groups (p<.01). The FTT children had lower birth weight and were more often small for gestational age. They were rated lower by their mothers on the 12 month health rating scale (p=.001) and were more likely to be judged suspect or abnormal on the neurological examination at all clinical visits. The FTT infants scored lower on the Bayley MDI & PDI at 12 & 24 months corrected age (p<.01).

In this large cohort of LBW, PT infant, followed longitudinally, several characteristics of the child, along with the quality of their home environments, differentiated the group of children with FTT from those without FTT.